

# THORACIC ENDOMETRIOSIS SYNDROME: IS IT AS RARE AS ONCE BELIEVED?

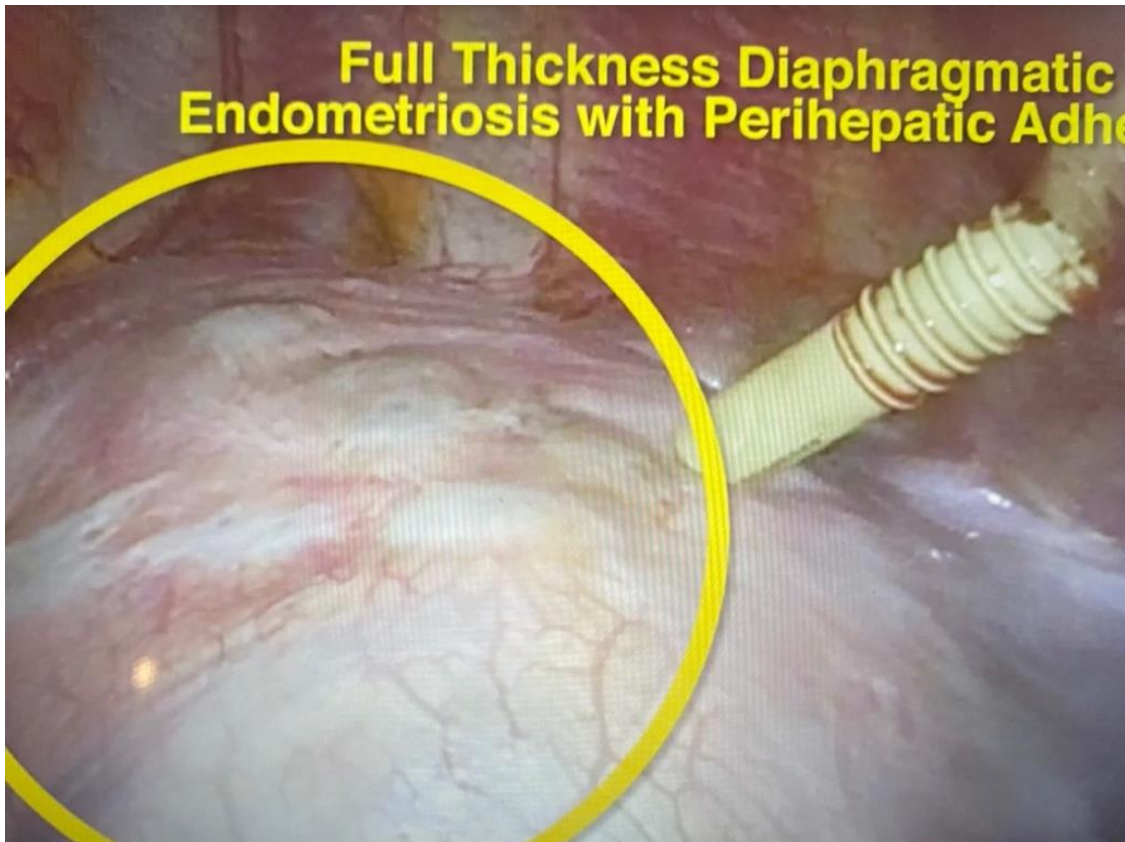
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**Thoracic Endometriosis Syndrome** was proposed by Joseph and Sahn (1996) and included clinical manifestations of thoracic endometriosis; mainly catamenial pneumothorax, hemothorax, hemoptysis, lung nodules, chest pain and pneumomediastinum. These conditions occur when [endometriosis](#) (tissue that is similar to, but biochemically different than native endometrium) grows outside the uterus, and in this case, involves the diaphragm, thoracic cavity or lung.



*Figure 1. Endometriosis on the thoracic side of the diaphragm.*

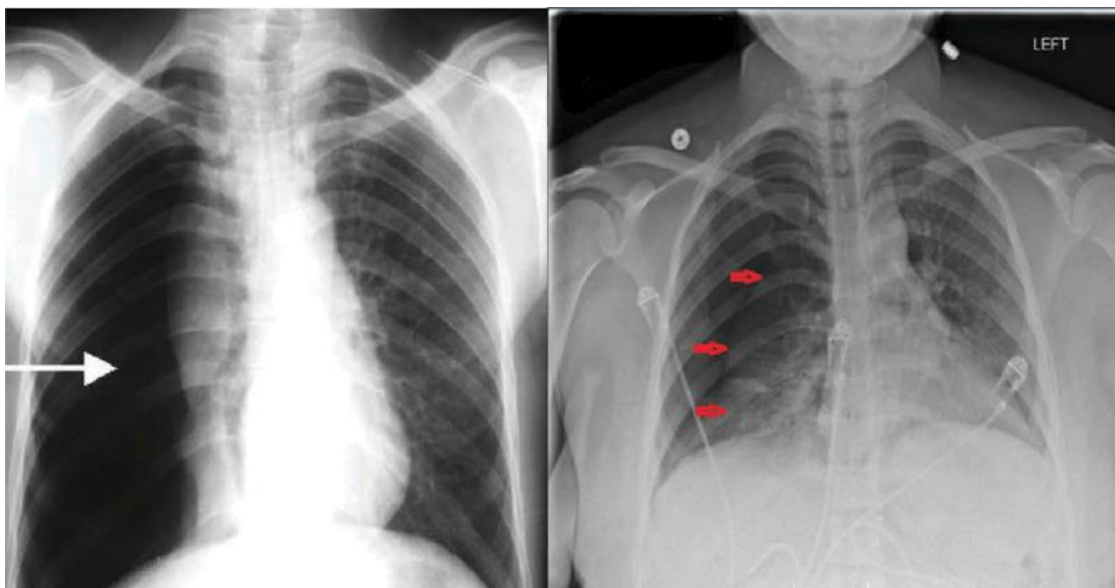
Most patients with thoracic endometriosis present with some form of chest pain. They may have collapses (both during and outside of their cycle), chest pain (either chest or scapular pain seen in over 90% of patients), coughing up blood (more often with their cycle), or collections of fluid into the chest (hydro- or hemo-thorax) that are not cancer related. The reason for patients experiencing upper chest pain usually has less to do with where the endo is located as it does with innervation of the diaphragm. The diaphragm is innervated by cranial nerves C3, 4 and 5. These nerves help with the motion of the diaphragm to help expand the lungs, but if there is pain from the diaphragm it is actually perceived in the shoulder blade, shoulder area and sometimes patients may have neck or even ear pain due to the shared innervation of the phrenic nerve. Often patients will initially only have their chest, shoulder, scapular and neck pain during their cycles. However, as the disease progresses, the pain may become continuous - often to the point that it is unrelenting, preventing patients from sleeping or even being able to function at all. The problem is, most do not respond to treatment in the area that it hurts, and PT, massage, acupuncture, trigger point injections, etc. all fail and when doctors try to find something on imaging focusing on those areas, they can never find anything. Other symptoms include shortness of breath, gurgling in the chest or upper abdomen, and cough.

**Table 1 – Symptoms of TES**

Chest Pain (either in lower ribcage or shoulder, scapular, neck or ear – usually unilateral but can be bilateral in a small percentage)
Shortness of Breath (in particular with pneumothorax)
Gurgling sensation in the lower chest
Cough/Coughing up blood
Orthopnea (Shortness of breath on lying down)

The most common manifestation is catamenial pneumothorax occurring in 72-73% of cases (Joseph and Sahn, 1996; Channabasavaiah and Joseph, 2010). “Catamenial” is derived from the Greek word “katamenios” which means monthly occurrence (Visouli et al., 2014). While spontaneous pneumothorax is thought to occur more commonly, at least 25-33% or more could be related to endo (Alifano et al., 2007; Härkki et al., 2010). This may reflect diagnosis bias, as many reviews of the literature are based in thoracic surgery. In a gynecologically initiated study by Nezhat et al. (2014) looking at 25 patients diagnosed during gynecologic surgery, catamenial pneumothorax was seen in only 24% of patients, while catamenial chest pain was seen in 80% and this was their only symptom in 40% of patients. We frequently see that as the primary symptom in well over half of the patients that present to us with a history of endometriosis and thoracic symptoms. Shoulder pain was seen in 40% of the patients, and hemoptysis in 12% in that study. As this was a gynecologically initiated study, diaphragmatic endo was seen in 100% of patients, and endometriosis was seen in 64% in the chest wall, and 40% of the lung parenchyma (lung tissue).

Similarly, in a study by Bobbio et al. (2017) looking specifically at non-pneumothorax cases of thoracoscopy at their center in women, they found chest pain (2/3), endo-related diaphragmatic hernia (20%) and endo-related effusion (fluid collections) in 16%. When excision and closure of the defect was performed, pain decreased from a mean of 8 to 3 post-op, long-term. With regards to diaphragmatic hernia, there were no recurrences after either closure or mesh. Patients treated for pleural effusions, with excision of endo and pleurectomy, had no recurrences. These suggest that a lot of women present with other symptoms than just pneumothorax.



**Figure 2. Pneumothorax can be seen on the patient’s right side of the chest, as evidenced by the area which is darker, reflecting lack of lung tissue and vasculature in the area (© Lateef et al., 2018).**

Of note, recently there have been studies looking at Thoracic-Endometriosis Related Pneumothorax (TERP) which includes women who were found to have endometriosis at the time of thoracoscopy or VATS. As many as a third (Alifano et al., 2007) had inter-menstrual (between cycles) pneumothorax, BUT as much as 63% had collapses between cycles in another study (Fukuoka et al., 2015).

Interestingly, all patients in the Fukuoka study were found to have endo on the diaphragm. In the period-related collapses, 62% also had endo on the chest wall lining (pleura), while those with non-period related collapses, only 44% were found to have endo involving the pleura. This suggests that the presence of endometriosis may have an effect at other times of the cycle as well and that the definition may need to be revisited, and the location of the endo may affect when the patient gets collapses. This also suggests two further ideas: not all collapses due to endo occur during a menstrual cycle, which means that both gynecologists and thoracic surgeons need to be more open to *ANY LUNG COLLAPSE* being due to due to endometriosis; and finally, we may need to get rid of the idea that we call women with collapses during the cycle Catamenial and instead include all potential women with collapses as having Thoracic-Endometriosis Related Pneumothorax (or more broadly including women with other presentations/manifestations and call it Thoracic Endometriosis Syndrome or TES).

Why do collapses occur? We do not know for sure, but several different theories have been proposed. The “physiologic hypothesis” suggests that vasoconstriction and bronchospasm, caused by higher levels of prostaglandin F<sub>2</sub> (an inflammatory mediator which is released from the uterus and endometriosis) may induce alveolar (small peripheral lung sacs where exchange of oxygen and CO<sub>2</sub> occur) rupture and subsequent pneumothorax. If there are pre-existing blebs or bullae (weakened distended areas of the lung), these may be more likely to rupture during the cycle. The absence of characteristic endometriosis lesions may support this theory in some patients (Visouli et al., 2014).

The next theory (microembolization theory) suggests that endometrial tissue can spread through venous or lymphatic system to distant locations, including the lung (Visouli et al., 2014). When these lesions implant in the lung periphery, where there is necrosis in that lung tissue, there is weakening of the lung parenchyma and rupture of the alveoli and collapse of the lung. This theory can also best be used to explain isolated pulmonary endometriosis nodules. If the embolized lesion occurs closer to the bronchi, it can result in hemoptysis or coughing up bloody fluid/phlegm. Sometimes, this can be voluminous.

The “transgenital-transdiaphragmatic” air passage theory suggests that air can pass from the vagina, cervix (which has less cervical mucous during menses), uterus, fallopian tubes and through the diaphragmatic fenestrations, which can be either congenital or as we feel, more secondary to endometriosis. This “LEAK” allows for air to get in the lung, and the normally sealed lung collapses and this repeats itself monthly, until the defects are completely removed. Recurrent collapses after hysterectomy, tubal ligation or complete resection of fenestrations and pleurodesis go against this theory for all collapses.

The retrograde menstruation theory suggests that the active lesions can be shed from the uterus and implant on the diaphragm, predominantly on the right side of the uterus due to the peritoneal “clockwise flow” of fluid within the abdomen. These implants can then create fenestrations or deeper nodules that can cause collapse or pain, and in severe cases, re-seed the chest to cause hemothorax. As well, the fluid within the chest can also be seen as ascites (or fluid within the abdomen) and can pass freely between the lung and abdomen in some patients. We sometimes see patients with endometriosis associated bloody ascites by itself, but can see patients with only chest related bloody fluid as well. There are several disadvantages to this theory, including poor evidence of the peritoneal flow of fluid in the abdomen, differences in the genetics and biochemistry of endometriosis and native endometrium (the cells shed from the uterus), lack of demonstration of actual implantation of live endometriosis cells, and a low recurrence rate (5-10%) following complete excision, while this theory would suggest should be close to 100% since most women continue to have retrograde menstruation unless they have had tubal ligation or hysterectomy (and recurrence after these procedures, which should not occur either).

Finally, the Mülleriosis theory (Redwine, 1988) suggests that endo is created following abnormal differentiation of the Müllerian duct system during embryogenesis, occurring as a result of malfunction of specific genes or possibly even mutations that can occur due to environmental exposures. The concept of mülleriosis is a broadened view of the embryonic rest theory advanced by Russell (1899) and others. It is different from Sampson's (1925) “Müllerianosis,” a term referring only to ectopic endometrial elements and that he considered and then discarded (Redwine, 1988).

The presence of endometriosis in stillborn fetuses occurring at a prevalence similar to that in the general population - close to 10% (Signorile et al., 2012) - and the biochemical differences seen in endometriosis and endometrium e.g. the presence of Aromatase (an estrogen-producing enzyme) in endometriosis and not endometrium supports this theory best of all (Delbandi et al., 2013). It also explains low recurrences following complete excision and the presence of disease on organs that are more difficult to explain otherwise.

Hemothorax is typically seen in a small percent of patients (less than 10%) and may be the most severe form of thoracic endometriosis, as many of these patients have extensive or near complete pleural involvement, quickly re-accumulating the bloody fluid that is drained. This is rare and should almost always be managed at a tertiary referral center with experience. There are few centers with any experience outside the CEC for this presentation.

Pulmonary nodules are diagnosed during imaging of the chest and often confused for other benign and malignant nodules. These occur 5-10% of the time. Hemoptysis is seen in more than 10% of patients and typically in younger patients than with other symptoms of thoracic endo. While hemoptysis patients are a mean of 25 years, patients with other forms of TES are closer to 35-38 years of age. While the mean is 35 years, cases have been reported in girls as young as 10 years of age as well as post-menopausal women.

Interestingly, women with catamenial or TERP may have a much higher rate or recurrence compared to women without endo-related pneumothorax or men. Mehta et al. (2016) found that as many as 64% of women after receiving initial treatment with chest tube, compared to only 5% of men having as recurrence. In those needing a second surgery, they were usually treated with pleurodesis after failed hormonal suppression (most studies suggest that at least 60% have a recurrence of collapse or pain within 6 months of stopping suppression, but these women had collapses with **DESPITE BEING ON SUPPRESSION**). Alifano et al. (2011) found that 45% that were re-operated on needed diaphragm resection, suggesting that either endo or fenestrations were not noted during the initial surgery. As well, only 5 out of 35 were found to have endo at initial surgery, while 18 out of 35 were found to have endo at repeat thoracoscopy, also suggesting that it was missed during the initial surgery. Haga et al. (2014) found recurrences in about 40% of patients, and those with glandular endo were much more likely to have recurrences (67%) than those without glandular endo found during initial surgery (38%).

It is felt that most women with thoracic endometriosis also have pelvic endometriosis. Tulandi et al. (2018), found 94% also had pelvic endometriosis, mainly stage III and IV; 60% had thoracic endo found at the time of collapse. Soriano et al. (2012) found that 85% had severe pelvic involvement with endometriosis in the TES patients that presented to their facility. For this reason we suggest that women have a combined approach with both laparoscopic excision of pelvic and sub-diaphragmatic endo and thoracic endometriosis with VATS. By having the 2 specialists there together, we minimize recurrences and have 2 experts ensuring all the disease is removed. As well, both procedures can be done at the same time, instead of exposing the patient to 2 surgeries, 2 intubations, and 2 recoveries.

Where do we usually find diaphragmatic endo? Most of the studies find over 90% on the right side of the chest. Bilateral cases are seen in as many as 10% and isolated left sided lesions being present less than a few percent of the time (Joseph and Sahn, 1996). Ceccaroni et al. (2013) looked at all the patients their institution had treated for diaphragmatic endo (DE). They found DE in 46/3008 patients (about 1.5%), which in and of itself is a lot more than expected for a “rare” disease – extrapolating that out to the USA, we could expect as many as 130,000 women with this problem, but this may also reflect that theirs is a large referral center. Multiple lesions are more common, with almost 70% having more than one lesion.

### ***Etiology of Thoracic Endometriosis***

We do not know the exact cause of thoracic or diaphragmatic endo; however, we do believe that most endo is best explained by either embryologic placement of endometriosis-like tissue or cells that have the ability to become endometriosis through a process called coelomic metaplasia, in which cells that have the ability to become endometriosis. There may be immunologic or genetic factors (but only 38% of identical twins both have it); environmental toxins may also play a small role.

Homeobox (HOX) genes – dysfunction of HOX genes may result in abnormal differentiation and migration of cells during embryonic formation of the female reproductive tract, giving rise later to endometriosis (Taylor et al., 1999). The presence of endometriosis in fetuses (Signorile et al., 2012) strongly suggests an embryologic origin as suggested over 30 years ago by the leading researcher and excision pioneer, [David B. Redwine, MD](#). In this theory as noted above, “Mülleriosis” is a developmental defect in the differentiation or migration of the any cellular component of the Müllerian duct system (the system that becomes the female reproductive tract and peritoneum) whether endometrial, myometrial, tubal or cervical; or coelomic epithelial anlage (embryologic precursor) of the adult.

### ***Diagnosis of Thoracic Endometriosis***

The diagnosis of endometriosis first has to consider the possibility of endometriosis occurring on the diaphragm and or in the chest - and that is the biggest problem, since most doctors (gynecologists, thoracic surgeons, pulmonologists and primary care doctors) think that it is so rare most do not even consider it as a possibility. But as the extrapolation above showed, it could be as many as 130,000 in the USA, but more realistically it is somewhere between 10,000 and 50,000 patients. Once we accept that the patient could have endo, what are some indicators that increase the likelihood? Recurrent pneumothoraces are commonly seen due to improper or inadequate treatment of the endometriosis within the chest or on the diaphragm. As well, pleurodesis may not be enough to help with recurrent pneumothoraces, and more aggressive treatment with pleurectomy (removal of the chest wall lining) may be needed to minimize the likelihood of recurrence. Progressive chest pain is a RED FLAG for possible diaphragmatic endo as well (in a patient with a history of pelvic endo or suspected pelvic endo). Chest pain that persists despite aggressive treatment in that area that hurts. Associated symptoms of cough, shortness of breath, especially with lying down, cyclic pain that is associated with the period (although it may start this way, it can become continuous over time). Neck and ear pain can be due to diaphragmatic endo.

### ***Imaging***

Unfortunately, most patients will have negative imaging for endo involving the chest, and they usually have to undergo extensive testing to rule out other causes of chest pain including cardiac workups with EKG, Holter Monitors and heart echo. As well, they usually end up getting gastroenterology workups which can include endoscopies, liver function workups, HIDA scans (especially if right upper quadrant abdominal pain), CT scans of the abdomen and other motility tests. Along the way, a pulmonologist may be involved performing CT scans of the chest, pulmonary function tests and potentially bronchoscopies. However, once all those tests are done and we are left with trying to diagnose possible diaphragmatic and thoracic endo, how do we proceed?

At a minimum, everyone should have a CXR (chest x-ray) performed to look for collapse of the lung or pneumonia. It may, rarely, demonstrate severe changes with hemothorax, or even more rarely tension pneumothorax in which the heart and opposite lung are being pushed over. There may be fluid at the bases, or loculations (pockets) of fluid within the lung if previous surgeries. A large loss of chest volume can occur from a massive diaphragmatic hernia.

Then if that is negative, we usually request a CT scan of the chest without contrast. This is less for diagnosing endo, and more to rule out other causes of chest pain (Rousset et al., 2014) and seeing nodules that could be present in the lung, and for seeing more subtle collapses of the lung. A CT scan can sometimes pick up endo within the chest, but it has to be a fairly large nodule, often more likely seen on the diaphragm or liver, and possibly a diaphragmatic hernia, which can be associated with endometriosis. Nodules of liver penetrating through the diaphragm may be seen in some cases or small defects in the diaphragm, occasionally being several centimeters in size. CT may also demonstrate liver lesions or other areas involving the chest wall, if large enough. Parietal nodules can also be seen along the chest wall in some cases, especially in cases of hemothorax.



*Figure 3. CT scan demonstrating right-sided pneumothorax (black area at 9-12 o'clock of image).  
(©Lateef et al., 2018)*

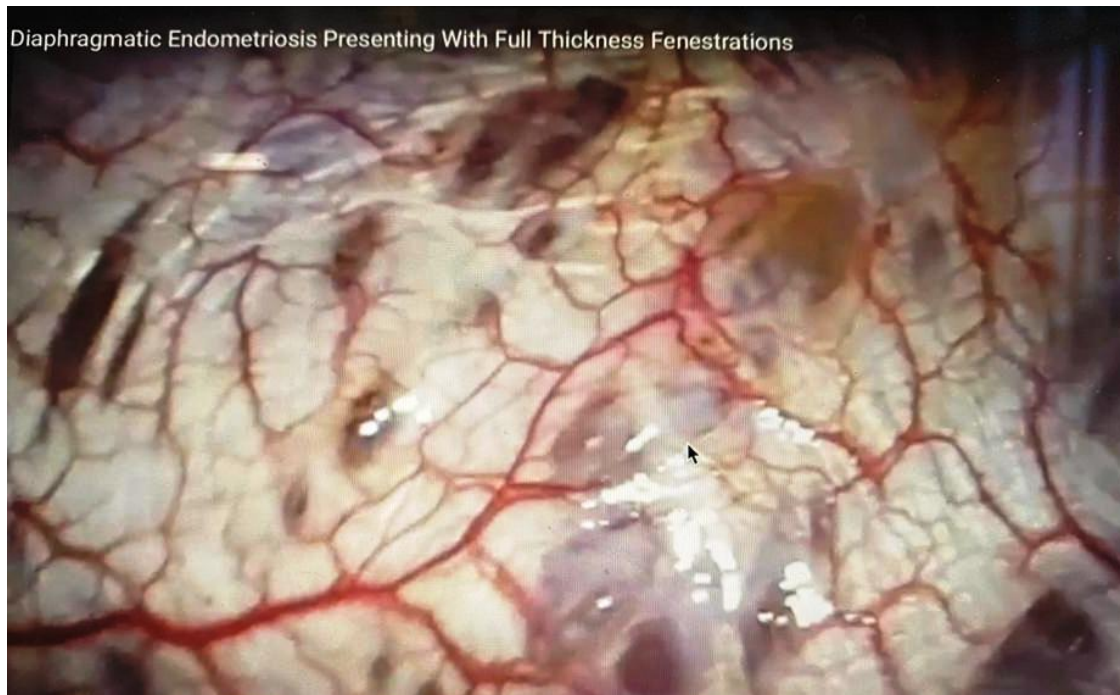
Finally, if possible, we attempt to get a thoracic MRI. This is best obtained by an in-network thoracic surgeon or pulmonologist, as they will meet less resistance from an insurance company if they order it, but there is good evidence supporting its use, especially in patients with recurrent pneumothorax or hemothorax, and in particular hemoptysis in a younger patient. Studies have shown that MRI can be fairly sensitive for picking up diaphragmatic endo in particular (78-83% sensitive), which are usually seen in the posterior and hyperintense on T1 weighting (Rousset et al., 2016).

### ***Treatment of Endometriosis-Related Thoracic Chest Pain***

#### **Pneumothorax/Chest Pain**

The management of patients with chest pain and catamenial pneumothorax is largely the same, except that patients without collapses do not need pleurodesis or pleurectomy.

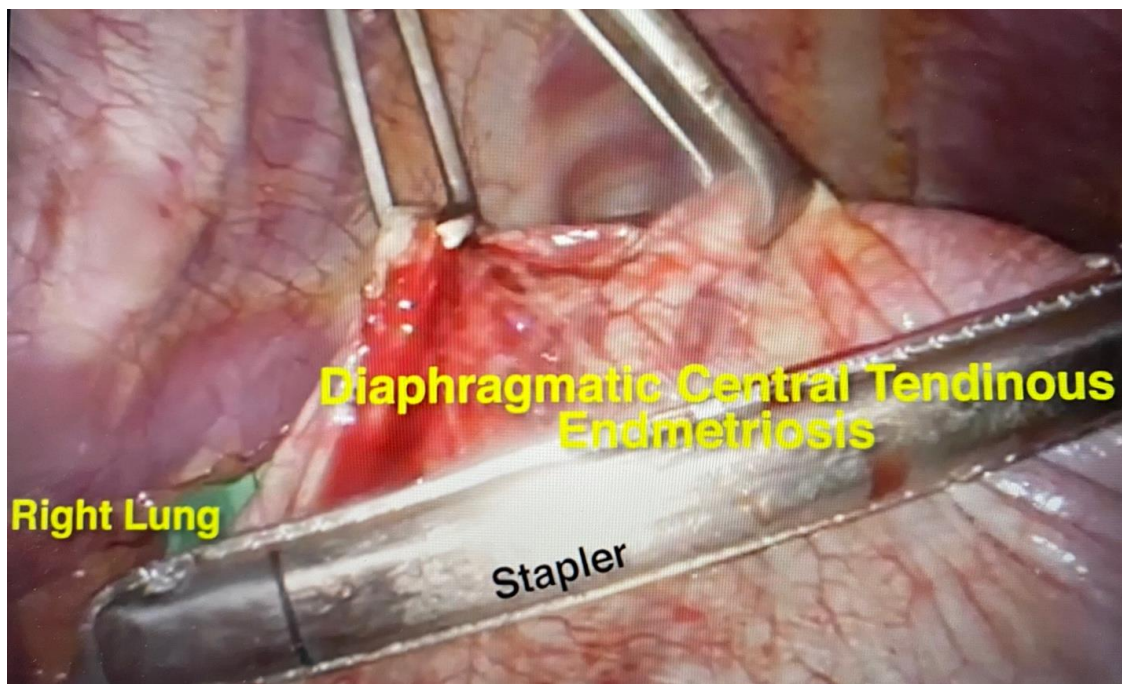
The initial management of pneumothorax is either observation in small collapses of the lung, or chest tube drainage. Patients with suspected endo-related collapses (and we should usually suspect this in all women with a history of endo or concomitant pelvic pain), are then usually treated with video-assisted thoracoscopic surgery which involves destruction of any seen endo (which is often not even looked for by most thoracic surgeons since they do not see this condition often) resection of blebs (weaknesses in the lung tissue which can cause a leak of the lung), and pleurodesis; endometriosis involving the surface of the lung or nodules as well. Pleurodesis is a process where the chest wall is roughened and made raw with a rough pad (mechanical pleurodesis) or a medicine/irritating substance is used (either talc or doxycycline/tetracycline) to cause an inflammatory reaction causing the lung to stick to the chest again. As can be seen in the above review, recurrences are common, despite these interventions.



**Figure 4. Diaphragmatic fenestrations or holes.**  
*All must be completely resected to ensure that no further collapses recur.*

Why do recurrent collapses occur? The main reason has to do with failure to recognize endometriosis as the cause of the collapse in women. When this failure happens, the endometriosis continues to affect the lung and diaphragm causing recurrent collapses. When a thoracoscopy is performed, the thoracic surgeon should be guided by a gynecologist trained in all appearances of endo (many of which missed by less trained gynecologists at least 25% of the time). We should be looking for lesions involving the diaphragm such as classic lesions of endo, but more importantly, fenestrations (holes) in the diaphragm as well as pleural lesions (since as many as 62% may have these lesions) and lung lesions (seen as high as 40% of the cases). All disease must be removed. That is why these surgeries are best performed by a multi-disciplinary team with both a trained gynecologist with thoracic endo experience, and a thoracic surgeon that has seen endo, treated it and had good results. This is validated by other studies as well (Visouli et al., 2012; Nezhat et al., 2014).

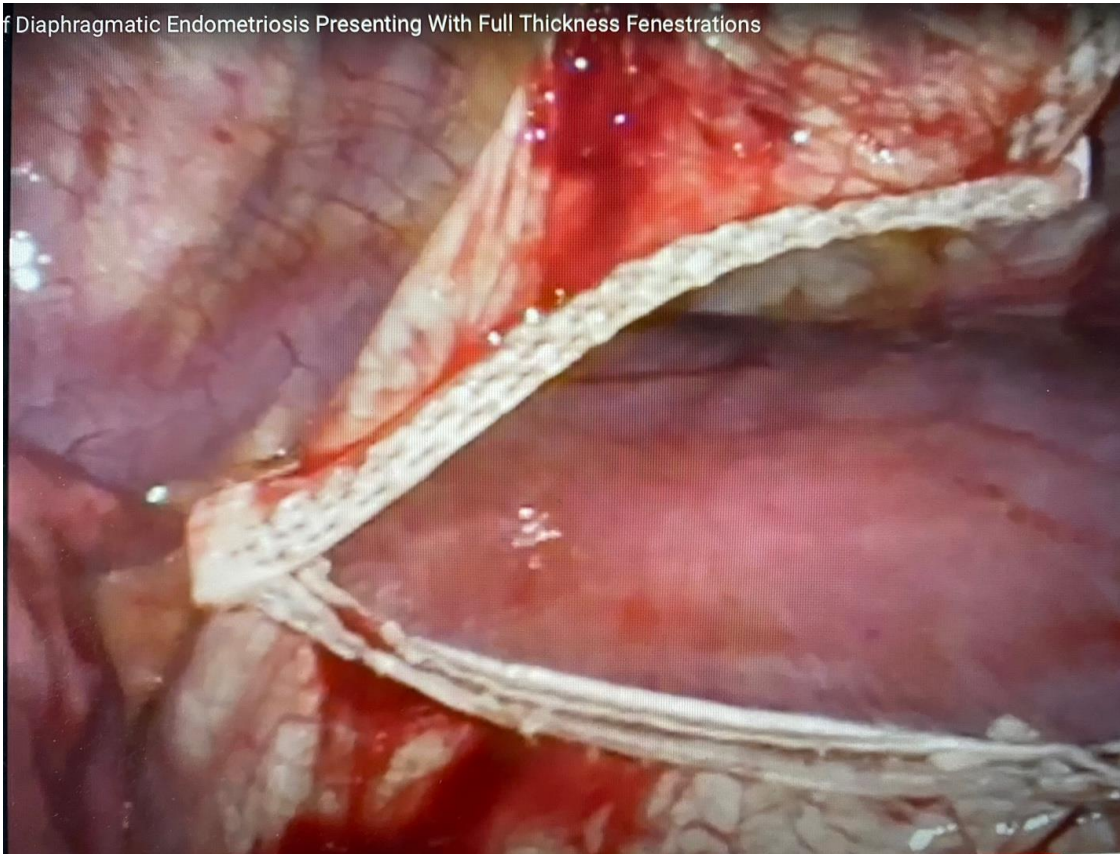
When we perform a combined laparoscopy and VATS, the gynecologist excises all the endo in the pelvis and diaphragm, and then excises the endo off the diaphragm from below. The patient must be placed in steep reverse Trendelenberg (foot down) position so that all of the diaphragm can be seen. We usually have to put a port immediately below the ribcage on the right side if pain on that side (which it usually is). Then, we can look with a 30 degree scope which allows us to see the very posterior aspect between the liver in the diaphragm. Alternatively, the falciform ligament separating the left and right sides of the liver/diaphragm can be cut allowing the liver to fall lower so it can be seen from the umbilical trocar. Once we have completely evaluated the diaphragm on both the right and left side and removed all the disease possible, we then re-position the patient and a VATS or thoracoscopy is performed and any remaining endo is removed and if there were collapses, a pleurodesis or pleurectomy is performed and any blebs or lung endo is removed.



*Figure 5. Stapler placed across the diaphragm below the fenestrations or endometriosis nodules and fired.*

Diaphragmatic fenestrations must be fully resected either by cutting out the area and oversewing the defect or by using a stapler. A mesh such as Gore-tex or a biologic mesh can be used, but only when a large defect is created. A mesh should not be used to cover the fenestrations since the endo will persist and lead to recurrences and potentially pain. If there are persistent symptoms after an overlying mesh, the mesh may become embedded into the diaphragm and impossible to remove. So if the surgeon suggests that they will use a mesh over the fenestrations, instead of excising them, then this option should be avoided. As well, the holes should not be over-sewn as this will leave disease behind and cause recurrent chest pain and increase the risk of recurrent pneumothorax as well. Disease should be removed and not just covered up. Electrocoagulation should be attempted to be avoided due to devascularization of the tissue which could result in coagulation-induced fenestrations, resulting in possible collapse or recurrent pain due to incomplete treatment of the endo with this approach (Nirgianakis et al, 2017).





**Figure 6. After stapler fired showing staple line and specimen (still attached before final stapling).**

Usually, a chest tube is inserted into the chest and it is removed when there is no further evidence of pneumothorax. If there are adhesions involving the lung to the chest from the previous pleurodesis or in cases, multiple pleurodeses, there is a chance of an air leak from the lung and it may take more than a day or 2 before the chest tube can be removed. Once the chest tube is removed, the patient is able to be discharged once pain is well managed. A chest x-ray is usually performed the day of chest tube removal and the day after, and usually repeated before returning home. Patients can fly home 5-7 days after surgery assuming no evidence of a recurrent collapse.

**WATCH:**

**[Multidisciplinary Approach for Resection of Diaphragmatic Endometriosis with Perihepatic Adhesions](#)**

**[Resection of Diaphragmatic Endometriosis Presenting With Full Thickness Fenestrations](#)**

When the endometriosis is excised, it should be examined by the pathologist. Typically, the pathologist will look microscopically for endometrial glands and stroma which are diagnostic of endometriosis. However, with diaphragmatic endometriosis, glandular elements are often not seen. There may be sheets of stromal cells. Often these are best seen with special stains such as CD10 which detects endometrial stroma (Guedj et al., 2009). Other studies have also found a high incidence of progesterone and estrogen receptor staining within diaphragmatic and thoracic endo, being as high as 100% in some studies (Haga et al., 2013). It would be beneficial to stain for these markers whenever endometriosis is suspected in any thoracic case.

## **Hemothorax**

Patients with hemothorax usually have the same treatment, except they almost always need pleurectomy to ensure that all the endo has been removed. As well, they may need a decortication of the lung, which involves removing the thick capsule that can occur from prolonged exposure to the endo and bloody inflammatory fluid that is present. The decortication may result in air leaks as well and may prolong the amount of time a chest tube is needed.

## **Hemoptysis**

While we always look in the bronchial cavity when we check for tube placement (perform a bronchoscopy), we can also assess the bronchi for any suspicious lesions suggestive of endo. This is particularly important when examining the patient for catamenial hemoptysis or coughing up blood. This is one situation where the area suspicious for endometriosis may need to be ablated, since the endo may be located in areas that are close to major blood vessels. The area can be washed to confirm the presence of endometrial cells or more commonly, hemosiderin laden macrophages. If there is heavy bleeding, an interventional radiologist may need to embolize (catheterize under x-ray guidance the blood vessels that are bleeding and shower the area with small particles that stop the bleeding) the affected area and prevent further bleeding in the future.

## **Post-Operative Suppression**

The use of post-operative suppression is very controversial. Most of the early studies recommended post-op suppression with strong medications such as Lupron, or Danazol (or more recently, possibly Orilissa). The early studies which had higher failure rates often did not involve complete excision of the endometriosis, usually ablating with cautery the endo that was found. There would be a much higher rate of recurrence when these early studies were performed since ablative therapies were often used and suppressive medication would likely have resulted in a much lower recurrence rate compared to excisional therapies. However, as many studies have demonstrated, there are still recurrences when suppression is used, especially after non-excisional treatment. When these medications are stopped, 50% recur within 6 months, and 60% recur within 12 months. These recurrences are for pneumothorax in particular. A recent study by Subotic et al. (2016), did not see any recurrent collapses in patients that had complete resection yet no post-op suppression for a number of reasons. This is consistent with our experience. We have only seen occasional collapses (<<10%) following complete excision and the need for suppression is questionable. They are usually small and can often be treated with a pig-tail catheter and localized pleurodesis. We definitely do not feel strong suppression such as Lupron, Orilissa or Danazol are required based on these findings. It may be reasonable to suppress ovulation for 3-6 immediately post-operatively, and this can usually be accomplished with either continuous low dose contraceptives or progestins such as norethindrone. Dienogest (Visanne), a progesterone that is only available in countries outside the USA as a standalone drug, may be better tolerated and more effective than other progestins (Fukuda et al., 2018), but there is a combination pill in the USA called Natazia, with estradiol valerate. These could be considered for patients on a longer term basis if well tolerated.

Very rarely, these treatments fail or when a mesh has made complete removal impossible, and despite trial of other hormonal treatments in that situation, more aggressive treatments are needed. In patients whom all other treatments have failed (which should happen less than a few percent of the time), consideration for possible total laparoscopic hysterectomy with bilateral salpingo-oophorectomy may be needed. In that case, it may be recommended to delay resumption of HRT until 6 months later to allow any residual minimal disease to atrophy and then low dose therapy reinstated to manage hypoestrogenic symptoms. The concurrent use of a progestin may be indicated to minimize any stimulation of possible residual endo. These types of recurrence are rare, and have been necessitated in less than 1-2% of more than 300 thoracic endo patients that have presented to our center.

## *Non-TES Causes of Chest Pain in Women*

### **Cardiac Causes of Chest Pain**

This is by far the most serious cause of chest pain that can be life threatening. This group of conditions includes Myocardial Infarction (MI), myocarditis, coronary heart disease, cardiomyopathy, and pericarditis. These are serious conditions that usually are detected early on in a diagnostic workup since most patients with cardiac symptoms have a full workup including EKG, cardiac enzymes, echocardiography and Holter monitoring which will almost always pick up these conditions. As women with heart disease may present atypically from men, there is a lower threshold for performing these tests. As well, women with heart disease may not have the typical cardiac arrest symptoms such as chest pain and they could include nausea, abdominal pain, pain radiating into the jaw, arms and legs, fatigue, heart palpitations, shortness of breath, cold sweats and anxiety. Each of these cardiac conditions is managed based on the cause, and some can be managed aggressively, and others may take time to resolve spontaneously, or when they progress too far, may require surgery.

### **Gastroenterologic Causes of Chest Pain**

**Gastroesophageal reflux disease (GERD).** GERD occurs when stomach acid refluxes or flows backwards from the stomach into the esophagus. This typically happens a few times a week and can be a nuisance or in more severe cases a severe cause of pain. It may account for as much as 2/3 of non-cardiac related chest pain and present as a burning sensation (heart burn), chest pain, difficulty swallowing or acid-like fluid in the esophagus or even mouth. There may be food in the fluid as well. This is not necessarily menstrual-related, and can even wake the patient at night and even cause reflux into the lung causing shortness of breath and chest tightening. An initial trial of PPI (proton pump inhibitors) called the omeprazole test can be tried, in which the patient takes a proton pump inhibitor—it does not matter whether it is omeprazole, lansoprazole, esomeprazole, or dexlansoprazole—twice daily for 1 week. If the patient has improvement, it is highly likely to be GERD. GERD is more definitely diagnosed with an endoscopy in which a flexible scope is inserted into the stomach while the patient is asleep. As well, esophageal manometry (pressure monitoring) and 24 hour pH testing may provide confirmation of GERD, but access to the test may be more difficult. With endoscopy, a gastroenterologist can diagnose the condition and rule out other causes of stomach/esophageal pain such as peptic ulcer disease and gastritis and prevent pre-cancerous and even cancerous changes that can occur when left untreated.

**Hiatal Hernia** is a condition in which there is a weakness in the diaphragm where the esophagus passes through it. This weakening allows the diaphragm to expand allowing the upper part of the stomach pass into the chest. Small hiatal hernias usually do not cause symptoms or problems, but larger ones can be problematic. Symptoms like heartburn, regurgitation of food into the esophagus, GERD, swallowing difficulties, abdominal and chest pain, shortness of breath, or even gastrointestinal bleeding. Patients that present with severe symptoms may require a hiatal hernia repair or Nissen fundoplication, which can be done laparoscopically.

**Gall Bladder Disease** can include not only gall stones, but biliary sludge, and dysfunction of the Gall Bladder. The Gall Bladder is an organ that sits below the right side of the liver and is responsible for storing bile, a product from the liver that is released into the small bowel to aid in digestion of the fats, when a hormone released from the stomach (CCK or cholecystokinin) stimulates contractions of the Gall Bladder. When the Gall Bladder does not function well, it can result in a condition called cholecystitis or inflammation of the gall bladder wall and on ultrasound of the abdomen, we can see thickening of the gall bladder wall. Sometimes we can see sludge (fine particulate matter that looks like super-fine sand) or even stones. We normally perform an ultrasound of the Gall Bladder to assess it for these conditions, but sometimes it may look perfectly normal – yet not function normally.

To assess the function of the Gall Bladder, we normally perform a HIDA scan in which a safe radioactive tracer is given to the patient. It accumulates in the liver and Gall Bladder, and CCK is given to cause the Gall Bladder to contract. Normally, the Gall Bladder ejects at least 35-50% of its contents. When it ejects less than this amount, it could be indicative of a condition called biliary dysfunction. All of these conditions in the setting of RUQ pain, suggest a Gall Bladder problem and removal of that organ (or cholecystectomy) would be indicated and helpful.

## **Pulmonary Causes of Chest Pain**

There are many causes of chest pain related to the lungs, but the most serious are cancer, which fortunately is not seen often in younger patients who may be candidates for endometriosis-related chest pain. This can usually be ruled out with CRX, CT scan and tumor markers.

After lung cancer, a serious condition to rule out is **pulmonary embolism (PE)** in which a blood clot that usually develops in the legs, breaks off and travels to the lung blocking off a part of the lung causing decreased flow to that area and resulting pain from ischemia. There are certain conditions that can increase the risk of PE such as estrogen-containing birth control use, coagulopathies or conditions which increase the risk of clotting such as Factor V Leiden deficiency, Protein S and C deficiency, Antithrombin III deficiency, MTHFR mutations to name a few. If a patient is immobilized due to travel or injury, the risk can be higher as well. PE is potentially a life-threatening condition in a small percent of patients and immediate resuscitation (oxygen, fluids, and medication to increase blood pressure) may be needed for less than 10%. It may be suspected when pulse oxygen measurement is low, or with EKG which demonstrates elevated heart rate (sinus tachycardia) and potentially changes of right heart strain as the heart attempts to pump blood through an obstructed area. It usually requires confirmation with either a spiral CT scan of the chest which can show the damaged area of the lung or less commonly with V/Q scan (ventilation/perfusion scans) or pulmonary angiogram (both of which are less commonly used now). PE is treated with anticoagulation such as heparin in unstable patients or the use of low molecular weight heparin injections, or other newer medications such as platelet inhibitors or medications that inhibit coagulation in patients that are at risk of recurrence such as those with atrial fibrillation. Coumadin, which is another blood thinner, is less commonly used due to need for measurement of bleeding parameters such as PT/PTT or INR.

**Pneumonia** is another potentially serious condition that can cause chest pain. Presentation is usually more acute than TES-related chest pain, but can occur repeatedly or may be more persistent if incompletely treated. This is usually diagnosed by blood work confirming infection (CBC) and either CXR or CT scan. Most of the time, it can be managed with oral antibiotics, but some forms may require intravenous antibiotics if a severe infection or resistant bacteria.

**Pleurisy or Pleuritis** is an inflammation of the lining of the chest wall that can cause severe chest pain. It is often considered a diagnosis of exclusion after other causes of chest pain have been ruled out. It is managed by treating the underlying condition, and may be diagnosed on CT scan when there is fluid seen in the chest. **Costochondritis** is a painful involving the joints between the ribs and the sternum or breast bone. It is usually made worse by chest movement, stretching, coughing and pressure on the joint. Costochondritis may radiate to the back or abdomen. Causes include trauma to the chest, infections, arthritis, and physical strain, rarely tumors. It is usually treated with NSAIDs, nerve modulating medications likely amitriptyline, narcotics if acute, steroids and physical therapy.

**Thoracic Outlet Syndrome (TOS)** is a rare condition which causes pain due to either the blood vessels or nerves passing between the first rib and clavicle (collar bone), resulting in compression of the nerve. Patients will usually feel pain in the shoulder or arm, and sometimes weakness in the hands or fingers as well. TOS can be the result of traumatic injury, physical stress or strain (weight-lifting), repetitive or stress-related injuries, congenital anomalies in the anatomy (such as an extra or cervical rib or extra or thicker scalene muscle of the neck), tumor in the upper chest or armpit, and less commonly, pregnancy. Symptoms other than pain or weakness include muscle wasting in the muscle pad of the thumb, numbness or tingling in the arm, hand or fingers, and change in color or cool sensation in the fingers or thumb.

TOS can be either vascular, neurogenic or unspecified/undetermined. As the names suggest, vascular TOS involves either veins or arteries being compressed below the clavicle causing blood flow changes. Neurogenic TOS involves nerve compression and results in muscle loss and weakness and potentially a weak grip. Some patients describe not being able to hold objects in the affected hand. There are a number of signs that may suggest TOS, including bluish discoloration of the fingers or white appearance due to poor flow often with associated coldness in the affected hand; swelling, heat or tenderness in the arm or shoulder due to clots; and weak or low pulses in the affected arm. There may also be prominent blood vessels in the arm, shoulder or neck.

Diagnosis may be suspected by symptoms, measurement of blood pressure in both arms with a significant difference, signs mentioned above, limited range of motion of the affected arm, weakness of the grip, tenderness at the clavicle or rarely mass in the area, difference in the anatomy involving the clavicle on one side. Raising the arm above the head may exacerbate the pain. Often, special studies are needed to evaluate the anatomy or nerve function. This can include CT scan, MRI, angiography or ultrasound to assess blood flow, EMG or electromyography to assess muscle activity and nerve conduction studies.

Treatment includes physical therapy, use of NSAIDs, pain medications, muscle relaxants, and anti-coagulants (blood thinners) if a clot. Brachial Plexus Nerve blocks may help if the scalene muscle is abnormal. If benefit is seen, Botox may help decrease the size/activity of the muscle and help more long term. Often, surgical treatment may be needed, which may involve correction of the anatomy or removal of a rib, or possible repair of blood vessels. The exact approach depends on the surgeon's training, specific type of damage (vasculature or nervous) and preferred route of access.

**Asthma** (or reactive airway disease) is usually associated with shortness of breath, but can also cause chest pain. Asthma occurs when there is constriction or narrowing of the lining of the airways to the lungs from the nose and mouth. Asthma may be exercise-induced or caused by trigger such as allergens, dust, cold air, pollen, mold and even medications like NSAIDs. In addition to difficulty breathing due to the airway constriction, there can also be an increase in mucous, resulting in coughing and chest tightness and chest pain or aching. Patients may wheeze or make a high-pitched sound while struggling to get enough air. This is usually assessed by having pulmonary function tests before and after taking inhaled medications aimed at reducing the muscle inflammation such as bronchodilators, and steroids which must be taken daily to help minimize the response to some triggers and make the airways less reactive in the long-term. Steroids may sometimes have to be taken for acute exacerbations either orally or even intravenously in patients with severe disease.

**Panic attacks** are sudden bouts of intense anxiety or fear that may be associated with physiologic symptoms such as shortness of breath, heart palpitations, and chest pain as well as a sense of impending doom. It is a common reason for admission to the Emergency Department, and the patient may feel like they are having a heart attack. If there is any concern about a heart attack, it is imperative to get to the Emergency Room to rule it out, and if ruled out and patient responds to anxiolytic medications (anti-anxiety medications such as Ativan, valium or Xanax), then it may suggest panic attacks as a cause and the patient may need to identify the triggers associated with them, and how to best avoid them, or better, deal with them with behavioral techniques that are aimed at de-escalating the physiologic symptoms associated with them. This may require seeing their primary care doctor, psychologist and psychiatrist.

There are a number of other potential causes of chest pain that may need to be ruled out, but this is a list of more common causes.

### *In Summary*

Thoracic Endometriosis Syndrome is a group of painful chest conditions resulting from the deposition and growth of endometriosis on the diaphragm, chest wall, and lung. It is best treated with a multi-disciplinary team approach such as we use here in our Center, involving both gynecologist and thoracic surgeon to recognize and remove all the endometriosis that is present. Using this approach, we have an excellent chance of achieving pain relief with low chance of disease and symptom recurrence.

**Learn more about endometriosis at <http://centerforendo.com>.  
Interested in having Dr Sinervo review your case for potential  
treatment? Click [here](#)!**

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